Clinical trial results:
Immunogenicity Study of a DTaP-IPV-Hep B-PRP~T Combined Vaccine in Comparison to Infanrix Hexa™, Both Concomitantly Administered With Prevnar™ at 2, 4, and 6 Months of Age in Thai Infants.

Summary

EudraCT number	2011-004457-87
Trial protocol	Outside EU/EEA
Global end of trial date	19 November 2007

Results information

Result version number	v1 (current)
This version publication date	10 February 2016
First version publication date	31 July 2014

Trial information

Trial identification

Sponsor protocol code	A3L12

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00401531
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur, SA
Sponsor organisation address	1541, Avenue Marcel Mérieux, Marcy L'Etoile, France, 69280
Public contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001201-PIP01-11
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 August 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 November 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the hexavalent DTaP-IPV-Hep B-PRP~T combined vaccine induces an immune response that is at least as good as the response following Infanrix hexa™ in terms of seroprotection rates to Hep B and PRP, 1 month after a three-dose primary series (at 2, 4, and 6 months), when co-administered with Prevnar™.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. They were also followed up for a total of 300 days (including a 6 month safety follow up for SAEs) after the last vacine dose.

Background therapy:

All subjects in the study must have received Hep B vaccination at birth in order to comply with the Thai Standard Vaccination Schedule.

Evidence for comparator:

Infanrix hexa™ is a licensed DTap/Hib/IPV/Hep B vaccine given in a three doses primary series vaccination.

Actual start date of recruitment	22 October 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Thailand: 412
Worldwide total number of subjects	412
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	412
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study participants were enrolled from 22 October 2006 to 19 November 2007 in 4 clinical centers in Thailand

Pre-assignment

Screening details:

Only participants who met all the inclusion, but none of the exclusion criteria were enrolled and vaccinated

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Blinding implementation details:

The investigator (blind observer or assessor) and subject's parents or guardians did not know the vaccine administered. The assessor was in charge of the assessment of safety held in a separate room and away from where the vaccines were prepared. A nurse/vaccinator was in charge of the preparation and administration of the vaccine(s) in another room away from the assessor. When necessary the scratch off emergency decoding procedure described in the study protocol were to be followed.

Arms

Are arms mutually exclusive?	Yes
Arm title	DTaP-IPV-Hep B-PRP-T + Prevnar™

Arm description:

Participants received a 3-dose primary vaccination series of diphtheria, tetanus, pertussis (2 component acellular), recombinant hepatitis B Hansenula and poliovirus vaccine adsorbed, and Haemophilus influenzae type B vaccine, conjugated to tetanus protein (DTaP-IPV-Hep B-PRP-T) vaccine co-administered with Prevnar vaccine (at 2, 4, and 6 months of age). All participants had received hepatitis B vaccination at birth.

Arm type	Experimental
Investigational medicinal product name	Hexaxim
Investigational medicinal product code	DTaP-IPV-HepB-PRP-T vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, at 2, 4, and 6 months of age.

Arm title	Infanrix Hexa™ + Prevnar™

Arm description:

Participants received a 3-dose primary vaccination series of Infanrix hexa vaccine co-administered with Prevnar vaccine (at 2, 4, and 6 months of age). All participants had received hepatitis B vaccination at birth.

Arm type	Active comparator
Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	Infanrix hexa™
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL at 2, 4, and 6 months of age.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The study was designed to have the investigator (blind observer or assessor) and subject's parents or guardians masked for the study vaccine administered to the participants.

Number of subjects in period 1	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™
Started	206	206
Completed	197	196
Not completed	9	10
Consent withdrawn by subject	3	2
Adverse event, non-fatal	2	-
Lost to follow-up	1	1
Protocol deviation	3	7

Baseline characteristics

Reporting groups	
Reporting group title	DTaP-IPV-Hep B-PRP-T + Prevnar™
Reporting group description:	
Participants received a 3-dose primary vaccination series of diphtheria, tetanus, pertussis (2 component acellular), recombinant hepatitis B Hansenula and poliovirus vaccine adsorbed, and Haemophilus influenzae type B vaccine, conjugated to tetanus protein (DTaP-IPV-Hep B-PRP-T) vaccine co-administered with Prevnar vaccine (at 2, 4, and 6 months of age). All participants had received hepatitis B vaccination at birth.	
Reporting group title	Infanrix Hexa™ + Prevnar™
Reporting group description:	
Participants received a 3-dose primary vaccination series of Infanrix hexa vaccine co-administered with Prevnar vaccine (at 2, 4, and 6 months of age). All participants had received hepatitis B vaccination at birth.	

Reporting group values	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™	Total
Number of subjects	206	206	412
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	206	206	412
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	1.88	1.9	
standard deviation	± 0.17	± 0.187	-
Gender categorical Units: Subjects			
Female	94	111	205
Male	112	95	207

End points

End points reporting groups

Reporting group title	DTaP-IPV-Hep B-PRP-T + Prevnar™

Reporting group description:

Participants received a 3-dose primary vaccination series of diphtheria, tetanus, pertussis (2 component acellular), recombinant hepatitis B Hansenula and poliovirus vaccine adsorbed, and Haemophilus influenzae type B vaccine, conjugated to tetanus protein (DTaP-IPV-Hep B-PRP-T) vaccine co-administered with Prevnar vaccine (at 2, 4, and 6 months of age). All participants had received hepatitis B vaccination at birth.

Reporting group title	Infanrix Hexa™ + Prevnar™

Reporting group description:

Participants received a 3-dose primary vaccination series of Infanrix hexa vaccine co-administered with Prevnar vaccine (at 2, 4, and 6 months of age). All participants had received hepatitis B vaccination at birth.

Primary: Number of Participants Achieving Seroprotection Against Hepatitis B and Haemophilus Influenzae Type b Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point title	Number of Participants Achieving Seroprotection Against Hepatitis B and Haemophilus Influenzae Type b Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point description:

Anti-Hepatitis B antibodies were measured using chemiluminescence detection technology; seroprotection was defined as a titer ≥ 10 mIU/mL. Anti-Haemophilus influenzae type b (anti-PRP) antibodies were measured by radioimmunoassay; seroprotection was defined as a titer ≥ 0.15 µg/mL.

End point type	Primary

End point timeframe:

Day 150 post-dose 1

End point values	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	190		
Units: Participants				
Anti-Hepatitis B	187	189		
Anti-PRP	183	183		

Statistical analyses

Statistical analysis title	Non inferiority of Hep B Seroprotection

Statistical analysis description:

The differences in seroprotection rates for the Hep B and PRP antigens between the two groups (Test – Control) were calculated. The non inferiority margin for Hep B and PRP antigens was set to be –10%. The statistical method was based on the lower bound of the two sided 95% confidence interval (CI) of the difference of the seroprotection rates.

Comparison groups	Infanrix Hexa™ + Prevnar™ v DTaP-IPV-Hep B-PRP-T + Prevnar™
Number of subjects included in analysis	379
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	> 10 [2]
Method	Wilson score
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.46
upper limit	2.43

Notes:

[1] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe. For each antigen, non inferiority for valence i was to be demonstrated if the lower limit of the two sided 95% CI was greater than -10.
The primary objective (non inferiority of the investigational DTaP IPV Hep B PRP T vaccine) was not rejected for the Hep B and PRP since the lower bounds were > -10%.
[2] - P-value was set at > -10%.

Statistical analysis title	Non inferiority of PRP Seroprotection

Statistical analysis description:

The differences in seroprotection rates for the Hep B and PRP antigens between the two groups (Test – Control) were calculated. The non-inferiority margin for Hep B and PRP antigens was set to be –10%. The statistical method was based on the lower bound of the two sided 95% confidence interval (CI) of the difference of the seroprotection rates.

Comparison groups	Infanrix Hexa™ + Prevnar™ v DTaP-IPV-Hep B-PRP-T + Prevnar™
Number of subjects included in analysis	379
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	> 10 [4]
Method	Wilson score
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	5.51

Notes:

[3] - The 95% CI was calculated based on the Wilson score method without continuity correction as described by Newcombe. For each antigen, non-inferiority for valence i was to be demonstrated if the lower limit of the two sided 95% CI was greater than -10.
The primary objective (non-inferiority of the investigational DTaP IPV Hep B PRP T vaccine) was not rejected for the Hep B and PRP since the lower bounds were > -10%.
[4] - P-value was set at > -10%

Secondary: Number of Participants With Seroprotection Against Diphtheria and Tetanus Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point title	Number of Participants With Seroprotection Against Diphtheria and Tetanus Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point description:

Anti-Diphtheria antibodies were measured by a toxin neutralization test. Anti-Tetanus antibodies were measured by an indirect enzyme-linked immunosorbent assay (ELISA). Seroprotection was defined for

both as a titer ≥ 0.01 IU/mL.

End point type	Secondary

End point timeframe:

Day 150 post-dose 1

End point values	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	190		
Units: Participants				
Anti-Diphtheria	184	190		
Anti-Tetanus	189	190		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Seroprotection Against Poliovirus Types 1, 2, and 3 Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point title	Number of Participants With Seroprotection Against Poliovirus Types 1, 2, and 3 Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point description:

Anti poliovirus types 1, 2, and 3 antibodies were measured by neutralization assay. Seroprotection was defined as a titer ≥ 8 1/dil

End point type	Secondary

End point timeframe:

Day 150 post-dose 1

End point values	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	186		
Units: Participants				
Anti-Polio Type 1	187	186		
Anti-Polio Type 2	187	186		
Anti-Polio Type 3	187	185		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Seroconversion Against Pertussis Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point title	Number of Participants With Seroconversion Against Pertussis Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point description:

Anti pertussis toxoid (PT) and anti-filamentous hemagglutinin (FHA) antibodies were measured by enzyme linked immunosorbent assay (ELISA). Seroconversion was defined as ≥ 4 fold increase over baseline.

End point type	Secondary

End point timeframe:

Day 150 post-dose 1

End point values	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	190		
Units: Participants				
Anti-Pertussis toxoid	177	177		
Anti-Filamentous hemagglutinin	177	179		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Vaccine Antibodies Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point title	Geometric Mean Titers (GMTs) of Vaccine Antibodies Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point description:

Anti-hepatitis B antibodies were measured using chemiluminescence detection technology. Anti-Haemophilus influenzae type b (anti-PRP) antibodies were measured by radioimmunoassay, anti-Diphtheria by toxin neutralization assay, anti-Tetanus and anti-Pertussis by enzyme-linked immunosorbent assay (ELISA), and anti-Polio by neutralization assay.

End point type	Secondary

End point timeframe:

Day 150 post-dose 1

End point values	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	190		
Units: titre				
geometric mean (confidence interval 95%)				
Anti-Hepatitis B	2477 (2044 to 3002)	2442 (2096 to 2844)		
Anti-PRP	5.07 (4.05 to 6.33)	2.41 (1.95 to 2.98)		
Anti-Diphtheria	0.297 (0.241 to 0.367)	0.209 (0.177 to 0.247)		
Anti-Tetanus	1.38 (1.25 to 1.52)	1.83 (1.69 to 1.97)		
Anti-Polio Type 1	765 (649 to 902)	1566 (1326 to 1850)		
Anti-Polio Type 2	1489 (1259 to 1761)	2277 (1905 to 2723)		
Anti-Polio Type 3	837 (695 to 1007)	2029 (1646 to 2502)		
Anti-Pertussis toxoid	168 (154 to 183)	200 (185 to 216)		
Anti-Filamentous hemagglutinin	148 (136 to 162)	123 (113 to 132)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting Solicited Injection Site and Systemic Reactions Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point title	Number of Participants Reporting Solicited Injection Site and Systemic Reactions Post-vaccination With Either DTaP-IPV-Hep B-PRP~T + Prevnar™ or Infanrix Hexa™ + Prevnar™

End point description:

Solicited Injection Site Reactions: Pain, Erythema, and Swelling. Solicited Systemic Reactions: Pyrexia, Vomiting, Crying, Somnolence, Anorexia, and Irritability Grade 3: Pain, cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥5 cm.
Grade 3: Pyrexia, >39°C; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying, >3 hours; Somnolence, Sleeping most of the time or difficult to wake up; Anorexia, Refuses ≥3 feeds/meals or refuses most feeds/meals; and Irritability, Inconsolable.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-vaccination

End point values	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	206		
Units: Participants				
Injection site Pain post-dose 1	161	135		
Injection site Pain post-dose 2	136	118		
Injection site Pain post-dose 3	119	112		
Injection site Pain post-any dose	180	166		
Grade 3 Injection site Pain post-any dose	20	12		
Injection site Erythema post-dose 1	79	64		
Injection site Erythema post-dose 2	93	91		
Injection site Erythema post-dose 3	86	79		
Injection site Erythema post-any dose	121	114		
Grade 3 Injection site Erythema post-any dose	3	2		
Injection site Swelling post-dose 1	59	34		
Injection site Swelling post-dose 2	52	44		
Injection site Swelling post-dose 3	34	32		
Injection site Swelling post-any dose	85	65		
Grade 3 Injection site Swelling post-and dose	1	1		
Pyrexia post-dose 1	109	68		
Pyrexia post-dose 2	84	79		
Pyrexia post-dose 3	81	81		
Pyrexia post-any dose	152	131		
Grade 3 Pyrexia post-any dose	6	7		
Vomiting post-dose 1	47	56		
Vomiting post-dose 2	28	32		
Vomiting post-dose 3	22	28		
Vomiting post-any dose	77	82		
Grade 3 Vomiting post-any dose	1	3		
Crying post-dose 1	128	106		
Crying post-dose 2	106	104		
Crying post-dose 3	77	75		
Crying post-any dose	167	153		
Grade 3 Crying post-any dose	7	5		
Somnolence post-dose 1	109	104		
Somnolence post-dose 2	91	79		
Somnolence post-dose 3	55	59		
Somnolence post-any dose	141	125		
Grade 3 Somnolence post-any dose	4	0		
Anorexia post-dose 1	59	49		
Anorexia post-dose 2	44	40		
Anorexia post-dose 3	36	37		
Anorexia post-any dose	91	83		
Grade 3 Anorexia post-any dose	0	0		
Irritability post-dose 1	134	122		
Irritability post-dose 2	107	109		
Irritability post-dose 3	90	88		
Irritability post-any dose	162	159		

Grade 3 Irritability post-any dose	4	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected following vaccination (Day 0) up to 10 months post-vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	DTaP-IPV-Hep B-PRP-T + Prevnar™

Reporting group description:

Participants received a 3-dose primary vaccination series of diphtheria, tetanus, pertussis (2 component acellular), recombinant hepatitis B Hansenula and poliovirus vaccine adsorbed, and Haemophilus influenzae type B vaccine, conjugated to tetanus protein (DTaP-IPV-Hep B-PRP-T) vaccine co-administered with Prevnar vaccine (at 2, 4, and 6 months of age). All participants had received hepatitis B vaccination at birth.

Reporting group title	Infanrix Hexa™ + Prevnar™

Reporting group description:

Participants received a 3-dose primary vaccination series of Infanrix hexa vaccine co-administered with Prevnar vaccine (at 2, 4, and 6 months of age). All participants had received hepatitis B vaccination at birth.

Serious adverse events	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 206 (2.91%)	8 / 206 (3.88%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 206 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	1 / 206 (0.49%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	1 / 206 (0.49%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	1 / 206 (0.49%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioneurotic Oedema			
subjects affected / exposed	1 / 206 (0.49%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema Herpeticum			
subjects affected / exposed	0 / 206 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 206 (0.00%)	3 / 206 (1.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 206 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			

subjects affected / exposed	1 / 206 (0.49%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethritis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 206 (0.49%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	DTaP-IPV-Hep B-PRP-T + Prevnar™	Infanrix Hexa™ + Prevnar™	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	161 / 206 (78.16%)	135 / 206 (65.53%)	
Nervous system disorders			
Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed	109 / 206 (52.91%)	104 / 206 (50.49%)	
occurrences (all)	109	104	
General disorders and administration site conditions			
InjectionsSite erythema			
alternative assessment type: Systematic			
subjects affected / exposed	93 / 206 (45.15%)	91 / 206 (44.17%)	
occurrences (all)	93	91	
Injection Site Pain			
alternative assessment type: Systematic			
subjects affected / exposed	161 / 206 (78.16%)	135 / 206 (65.53%)	
occurrences (all)	161	135	
Injection site swelling			
alternative assessment type: Systematic			

subjects affected / exposed	59 / 206 (28.64%)	44 / 206 (21.36%)	
occurrences (all)	59	44	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	134 / 206 (65.05%)	122 / 206 (59.22%)	
occurrences (all)	134	122	
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	109 / 206 (52.91%)	68 / 206 (33.01%)	
occurrences (all)	109	68	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 206 (3.40%)	13 / 206 (6.31%)	
occurrences (all)	7	13	
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	47 / 206 (22.82%)	56 / 206 (27.18%)	
occurrences (all)	47	56	
Psychiatric disorders			
Crying			
alternative assessment type: Systematic			
subjects affected / exposed	128 / 206 (62.14%)	106 / 206 (51.46%)	
occurrences (all)	128	106	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	31 / 206 (15.05%)	35 / 206 (16.99%)	
occurrences (all)	31	35	
Upper Respiratory Tract Infection			
subjects affected / exposed	45 / 206 (21.84%)	46 / 206 (22.33%)	
occurrences (all)	45	46	
Metabolism and nutrition disorders			
Anorexia			
alternative assessment type: Systematic			
subjects affected / exposed	59 / 206 (28.64%)	49 / 206 (23.79%)	
occurrences (all)	59	49	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2006	The amendment included in the version 3.0 of the protocol include changes in the logistics of the supply of the investigational and control vaccines and the handling of blood samples.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not applicable.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/21334243